Devi, S.
08/905046

Seq. ID 2

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     FILE 'REGISTRY' ENTERED AT 15:51:27 ON 16 JUN 2000
L1             4 S SAVALTYS/SQSP

L1   ANSWER 1 OF 4  REGISTRY  COPYRIGHT 2000 ACS
RN   203004-45-9  REGISTRY
CN   L-Proline, L-prolyl-L-seryl-L-alanyl-L-valyl-L-alanyl-L-leucyl-L-
     threonyl-L-tyrosyl-L-seryl- (9CI)  (CA INDEX NAME)
SQL  10

SEQ      1 PSAVALTYSP
            ========
HITS AT:   2-9

REFERENCE   1:  128:166357

L1   ANSWER 2 OF 4  REGISTRY  COPYRIGHT 2000 ACS
RN   203004-39-1  REGISTRY
CN   L-Serine, L-seryl-L-alanyl-L-valyl-L-alanyl-L-leucyl-L-threonyl-L-
     tyrosyl- (9CI)  (CA INDEX NAME)
SQL  8

SEQ      1 SAVALTYS
            ========
HITS AT:   1-8

REFERENCE   1:  128:166363

REFERENCE   2:  128:166357

L1   ANSWER 3 OF 4  REGISTRY  COPYRIGHT 2000 ACS
RN   186003-63-4  REGISTRY
CN   L-Alanine, L-cysteinyl-L-valyl-L-.alpha.-glutamyl-L-lysyl-L-
     asparaginyl-L-isoleucyl-L-threonyl-L-valyl-L-threonyl-L-alanyl-L-
     seryl-L-valyl-L-.alpha.-aspartyl-L-prolyl-L-threonyl-L-isoleucyl-L-
     .alpha.-aspartyl-L-leucyl-L-leucyl-L-glutaminyl-L-alanyl-L-.alpha.-
     aspartylglycyl-L-seryl-L-alanyl-L-leucyl-L-prolyl-L-seryl-L-alanyl-L-
     valyl-L-alanyl-L-leucyl-L-threonyl-L-tyrosyl-L-seryl-L-prolyl- (9CI)
     (CA INDEX NAME)
CI   MAN
SQL  37

SEQ      1 CVEKNITVTA SVDPTIDLLQ ADGSALPSAV ALTYSPA
                                          === =====
HITS AT:   28-35

REFERENCE   1:  127:148145

REFERENCE   2:  126:103107
```

L1 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2000 ACS
RN 186003-62-3 REGISTRY
CN L-Alanine, L-valyl-L-.alpha.-glutamyl-L-lysyl-L-asparaginyl-L-isoleucyl-L-threonyl-L-valyl-L-threonyl-L-alanyl-L-seryl-L-valyl-L-.alpha.-aspartyl-L-prolyl-L-threonyl-L-isoleucyl-L-.alpha.-aspartyl-L-leucyl-L-leucyl-L-glutaminyl-L-alanyl-L-.alpha.-aspartylglycyl-L-seryl-L-alanyl-L-leucyl-L-prolyl-L-seryl-L-alanyl-L-valyl-L-alanyl-L-leucyl-L-threonyl-L-tyrosyl-L-seryl-L-prolyl- (9CI) (CA INDEX NAME)
CI MAN
SQL 36

SEQ 1 VEKNITVTAS VDPTIDLLQA DGSALPSAVA LTYSPA
==== ====

HITS AT: 27-34

REFERENCE 1: 128:166363

REFERENCE 2: 128:166357

REFERENCE 3: 126:103107

FILE 'CAPLUS' ENTERED AT 15:52:08 ON 16 JUN 2000
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FILE COVERS 1967 - 16 Jun 2000 VOL 132 ISS 25
FILE LAST UPDATED: 15 Jun 2000 (20000615/ED)

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L2 4 L1

Searcher : Shears 308-4994

=> d 1-4 .bevstr

L2 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:112385 CAPLUS
DOCUMENT NUMBER: 128:166363
TITLE: Monoclonal antibody which agglutinates Escherichia coli having the CS4-CFA/I family protein
INVENTOR(S): Cassels, Frederick; Lees, Andrew; Schuman, Richard
PATENT ASSIGNEE(S): United States Dept. of the Army, USA; Virion Systems Inc.
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9805687	A1	19980212	WO 1997-US13477	19970801
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 918796	A1	19990602	EP 1997-938077	19970801
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1996-23075 19960802
WO 1997-US13477 19970801

AB A monoclonal antibody to a consensus peptide of the formula: VEKNITVTASVDPTIDLLQADGSALPSAVALTYSPA. The monoclonal antibody of the invention binds exclusively to the sequence SAVALTYS and has use as a diagnostic and for prophylaxis against illness arising from enterotoxigenic E. coli which produces CS4-CFA/I family of proteins and for treatment of disease arising therefrom.

IT **186003-62-3 203004-39-1**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(monoclonal antibody which agglutinates Escherichia coli having the CS4-CFA/I family protein)

L2 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:112247 CAPLUS
DOCUMENT NUMBER: 128:166357
TITLE: Peptides responsive to antibodies against a consensus peptide of the CS4-CFA/I family proteins
INVENTOR(S): Cassels, Frederick; Loomis-Price, Lawrance

PATENT ASSIGNEE(S): United States Dept. of the Army, USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9805348	A1	19980212	WO 1997-US13476	19970801
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 959895	A1	19991201	EP 1997-936322	19970801
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1996-23076 19960802
US 1996-23145 19960805
WO 1997-US13476 19970801

AB This invention relates to amino acid sequences from within a consensus peptide of the formula: VEKNITVTASVDPTIDLLQADGSALPSAVALTYS PA. Eight mer peptides from within the consensus peptide were tested against an antibody raised to the consensus peptide. Studies relating to antibody raised to denatured proteins from the natural organisms producing the family of proteins were also useful and showed particular value of some sequences. A sequence of the formula ASVDPTIDLLQA was identified thereby. An enlarge sequences of the formula TVTASVDPTIDLLQAD is also esp. interesting as are intermediate sequences such as sequences VTASVDPTIDLLQAD, TASVDPTIDLLQAD, and TASVDPTIDLLQA as being binding sites for antibodies raised to the denatured proteins. Peptides of the CS4-CFA/I family proteins is useful in providing needed vaccines specific against this class of enterotoxigenic or diarrheagenic Escherichia coli that pose great risk to travelers.

IT **186003-62-3 203004-39-1 203004-45-9**
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vaccine peptides responsive to antibodies against a consensus peptide of the CS4-CFA/I family proteins of enterotoxigenic diarrheagenic Escherichia coli)

L2 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:459893 CAPLUS
DOCUMENT NUMBER: 127:148145
TITLE: Antibody to N-terminal consensus peptide is cross-reactive with all six members of the enterotoxigenic E. coli CFA/I family
AUTHOR(S): Cassels, F. J.; Lees, A.; Hansen, B. D.;
Searcher : Shears 308-4994

Barringer, J. D.; Nelson, B. L.; Ryu, H.
CORPORATE SOURCE: Department of Gastroenterology, Walter Reed Army Institute of Research, Washington, DC, 20307, USA
SOURCE: Cytokines, Cholera Gut, [Pap. Jt. Meet. U. S.-Jpn. Coop. Med. Sci. Program Panels Malnutr. Cholera] (1997), Meeting Date 1995, 275-279. Editor(s): Keusch, Gerald T.; Kawakami, Masanobu. IOS Press: Amsterdam, Neth.
CODEN: 64SIAE
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The CFA/I family of enterotoxigenic Escherichia coli (ETEC) colonization factors (CF) consists of CFA/I, CS1, CS2, CS4, CS17, and PCF O166. They have been grouped as a family due to protein sequence homol. as well as immunol. cross-reactivity. In this study, addnl. protein sequence of CS2, CS4, CS17, and PCF O166 was obtained. From this sequence a consensus was derived, a thirty-six amino acid peptide corresponding to this consensus synthesized, the peptide conjugated to a carrier protein, and rabbits immunized. Sera tested pos. in an immunoblot (Western) assay against the peptide as well as against each of the members of the CFA/I family. The sera also agglutinated ETEC strains bearing CS1, CS2, and CFA/I in a slide agglutination test. These data demonstrate that a peptide derived from the consensus of the N-terminus of the CFA/I family is immunogenic and cross-reactive to each member of the family. It is hoped that these and addnl. studies may lead to a cross-protective vaccine to ETEC strains bearing these CF, as well as to a broadly reactive reagent useful in CF detection.
IT **186003-63-4**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cross reactivity of antibody to a consensus sequence peptide from the enterotoxigenic Escherichia coli CFA/I family)

L2 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:101598 CAPLUS
DOCUMENT NUMBER: 126:103107
TITLE: Methods of raising antibodies against Escherichia coli of the family CS4-CFA/1
INVENTOR(S): Cassels, Frederick; Anderson, Jeffrey; Carter, John Mark
PATENT ASSIGNEE(S): Department of the Army, US Government, USA
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9638171	A1	19961205	WO 1996-US8730	19960603
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5914114	A	19990622	US 1995-460617	19950602
CA 2223013	AA	19961205	CA 1996-2223013	19960603
EP 831900	A1	19980401	EP 1996-918041	19960603
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:			US 1995-460617	19950602
			WO 1996-US8730	19960603

AB A consensus peptide of 36 amino acids has been designed which acts as an immunogen raising antibodies against the proteins of all members of the E. coli family CS4-CFA/1. While the N-terminus of members of this family of organisms shows a high degree of identity, the remainder of the sequence of the proteins shows much less homol. across the strains. The region of the protein represented in the subunit encompasses known linear B- and T-cell epitopes of CFA/I. The consensus peptide has a high level of homol. to strains bearing six different colonization factors. The consensus peptide is of the formula: VEKNITVTASVDPTIDLLQADGSALPSAVALTYSPA. An alternative peptide, identified as consensus peptide 2 is of the formula: VEKNITVTASVDPTIDLLQADGSALPASVALTYSPA.

IT **186003-62-3 186003-63-4**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; peptide sequence for raising antibodies against Escherichia coli of the family CS4-CFA/1)

(FILE 'CAPLUS' ENTERED AT 15:52:08 ON 16 JUN 2000)

- key terms

L3 108342 SEA ABB=ON PLU=ON MOAB OR MAB OR MONOCLON? OR HYBRIDOM? OR 96109FE? OR 96(W)(109FE? OR 109 FE?) OR 12163 OR HB12163
L4 17 SEA ABB=ON PLU=ON L3 AND (CFA1 OR CFAI OR CFA(W)(1 OR I))
L5 6 SEA ABB=ON PLU=ON L4 AND (CS4 OR CS 4)
L6 5 SEA ABB=ON PLU=ON L5 NOT L2

R. Bradley; Svennerholm, Ann-Mari
CORPORATE SOURCE: Laboratory Sciences Division, ICDDR, Dhaka, 1000, Bangladesh
SOURCE: J. Clin. Microbiol. (2000), 38(1), 27-31
CODEN: JCMIDW; ISSN: 0095-1137
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The prevalence of toxin types and colonization factors (CFs) of enterotoxigenic Escherichia coli (ETEC) was prospectively studied with fresh samples (n = 4,662) obtained from a 2% routine surveillance of diarrheal stool samples over 2 yr, from Sept. 1996 to August 1998. Stool samples were tested by enzyme-linked

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L6 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:74547 CAPLUS
DOCUMENT NUMBER: 132:248318
TITLE: Prevalence of toxin types and colonization factors in enterotoxigenic Escherichia coli isolated during a 2-year period from diarrheal patients in Bangladesh
AUTHOR(S): Qadri, Firdausi; Das, Swadesh Kumar; Faruque, A. S. G.; Fuchs, George J.; Albert, M. John; Sack, R. Bradley; Svennerholm, Ann-Mari
CORPORATE SOURCE: Laboratory Sciences Division, ICDDR, Dhaka, 1000, Bangladesh
SOURCE: J. Clin. Microbiol. (2000), 38(1), 27-31
CODEN: JCMIDW; ISSN: 0095-1137
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The prevalence of toxin types and colonization factors (CFs) of enterotoxigenic Escherichia coli (ETEC) was prospectively studied with fresh samples (n = 4,662) obtained from a 2% routine surveillance of diarrheal stool samples over 2 yr, from Sept. 1996 to August 1998. Stool samples were tested by enzyme-linked immunoassay techniques and with specific **monoclonal** antibodies for the toxins and CFs. The prevalence of ETEC was 14% (n = 662), with over 70% of the strains isolated from children 0 to 5 yr of age, of whom 93% were in the 0- to 3-yr-old age range. Of the total ETEC isolates, 49.4% were pos. for the heat-stable toxin (ST), 25.4% were pos. for the heat-labile toxin (LT) only, and 25.2% were pos. for both LT and ST. The rate of ETEC isolation peaked in the hot summer months of May to Sept. and decreased in winter. About 56% of the samples were pos. for 1 or more of the 12 CFs that were screened for. The coli surface antigens **CS4**, CS5, and/or CS6 of the colonization factor antigen (CFA)/IV complex were

most prevalent (incidence, 31%), followed by **CFA/I** (23.5%) and coli surface antigens CS1, CS2, and CS3 of CFA/II (21%). In addn., other CFs detected in decreasing order were CS7 (8%), CS14 (PCFO166) (7%), CS12 (PCFO159) (4%), CS17 (3%), and CS8 (CFA/III) (2.7%). The ST- or LT- and ST-pos. ETEC isolates expressed the CFs known to be the most prevalent (i.e., **CFA/I**, CFA/II, and CFA/IV), while the strains pos. for LT only did not. Among children who were infected with ETEC as the single pathogen, a trend of relatively more severe disease in children infected with ST-pos. ($P < 0.001$) or LT- and ST-pos. ($P < 0.001$) ETEC isolates compared to the severity of the disease in children infected with LT only-pos. ETEC isolates was seen. This study supports the fact that ETEC is still a major cause of childhood diarrhea in Bangladesh, esp. in children up to 3 yr of age, and that measures to prevent such infections are needed in developing countries.

REFERENCE COUNT: 27

REFERENCE(S):
(10) Giron, J; Gene 1997, V192, P39 CAPLUS
(11) Giron, J; Mol Microbiol 1994, V12, P71 CAPLUS
(13) Levine, M; Infect Immun 1984, V44, P409 CAPLUS
(14) Lopez-Vidal, Y; J Clin Microbiol 1988, V26, P1967 CAPLUS
(15) Lopez-Vidal, Y; J Clin Microbiol 1990, V28, P1906 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1998:615639 CAPLUS

DOCUMENT NUMBER: 130:22754

TITLE: Epidemiology and properties of heat-stable enterotoxin-producing Escherichia coli serotype O169:H41

AUTHOR(S): Nishikawa, Y.; Helander, A.; Ogasawara, J.; Moyer, N. P.; Hanaoka, M.; Hase, A.; Yasukawa, A.

CORPORATE SOURCE: Department of Epidemiology, Osaka City Institute of Public Health and Environmental Sciences, Osaka, 543-0026, Japan

SOURCE: Epidemiol. Infect. (1998), 121(1), 31-42
CODEN: EPINEU; ISSN: 0950-2688

PUBLISHER: Cambridge University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Enterotoxigenic Escherichia coli (ETEC) serotype 0169:H41 organisms have become the most prevalent ETEC in Japan since the first outbreak in 1991. It was assumed that the outbreaks were due to clonal spread of this new ETEC serotype. The relationship of 32 strains isolated from 6 outbreaks were examd. for biotype,

antibiotic susceptibility, enterotoxigenicity, protein banding pattern, lipopolysaccharide banding pattern, plasmid anal., and ribotyping. Further, the strains were examd. by hemagglutination, surface hydrophobicity, and the ability to adhere to HEp-2 cells. The present study suggests that the outbreaks were caused by multiple clones of STp-producing 0169:H41 since they showed differences in ribotype and outer membrane protein banding patterns. The strains did not agglutinate human or bovine red blood cells in a mannose-resistant manner. They adhered to HEp-2 cells in a manner resembling enteroaggregative E. coli. Five strains were examd. by dot-blot tests for the colonization factor antigens **CFA/** I, CS1, CS2, CS3, **CS4**, CS5, CS6, CS7, PCFO159, PCFO166 and CFA/III. Although four strains expressed CS6, no structure for CS6 was identified. A strain that the anti-CS6 **MAbs** did not react with could adhere to HEp-2 cells in a mannose resistant manner; thus, it is unlikely that CS6 play an important role in the adhesion to the cells. Electron microscopy studies of the 0169:H41 strains suggested that curly fimbriae, a possible new colonization factor, may play an important role in the adhesion of the bacteria to HEp-2 cells. In conclusion, outbreaks due to ETEC 0169:H41 were caused by multiple clones, and the strains should be examd. in detail for a possible new colonization factor.

REFERENCE COUNT: 48

REFERENCE(S):

(2) Aubel, D; Infect Immun 1991, V59, P1290 CAPLUS

(3) Chart, H; J Gen Microbiol 1985, V131, P1503 CAPLUS

(6) Darfeuille-Michaud, A; Infect Immun 1986, V52, P468 CAPLUS

(7) Darfeuille-Michaud, A; Infect Immun 1990, V58, P893 CAPLUS

(11) Fitzgerald, S; Infect Immun 1980, V27, P302 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1996:502085 CAPLUS

DOCUMENT NUMBER: 125:165366

TITLE: **Monoclonal** antibodies against fimbrial subunits of colonization factor antigen I (**CFA/I**) inhibit binding to human enterocytes and protect against enterotoxigenic Escherichia coli expressing heterologous colonization factors

AUTHOR(S): Rudin, Anna; Olbe, Lars; Svennerholm, Ann-Mari

CORPORATE SOURCE: Department Medical Microbiology and Immunology, Goteborg University, Goeteborg, 413 46, Swed.

SOURCE: Microb. Pathog. (1996), 21(1), 35-45
CODEN: MIPAEV; ISSN: 0882-4010

Searcher : Shears 308-4994

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Enterotoxigenic E. coli (ETEC) bind to enterocytes in the small intestine by antigenically distinct colonization factors (CFs). By immunizing with isolated subunits of **CFA/I** fimbriae the authors have previously produced **monoclonal** antibodies (**MAbs**) that cross-react immunol. in vitro with several CFs. Two of these **MAbs** [S(subunit)-**CFA/I** 17:8 and S-**CFA/I** 5:6] were found to inhibit the binding of ETEC strains expressing either homologous or heterologous CFs, i.e. **CFA/I** and **CS4**, to isolated human jejunal enterocytes. The 2 **MAbs** also conferred passive protection against fluid accumulation in rabbit ileal loops caused by **CFA/I**- as well as **CS4**-expressing ETEC strains. Immunoelectron microscopy studies showed that both **MAbs** bound specifically to **CFA/I** as well as to **CS4** fimbriae expressed on bacteria. These results indicate the possibility to induce anti-CF antibodies that can protect against ETEC infection caused by bacteria expressing not only homologous but also heterologous CFs, by immunizing with fimbrial subunits.

L6 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1994:628215 CAPLUS
DOCUMENT NUMBER: 121:228215
TITLE: **Monoclonal** antibodies against enterotoxigenic Escherichia coli colonization factor antigen I (**CFA/I**) that cross-react immunologically with heterologous CFAs
AUTHOR(S): Rudin, Anna; McConnell, Moyra M.; Svennerholm, Ann-Mari
CORPORATE SOURCE: Dep. Med. Microbiology Immunology, Univ. Goeteborg, Goeteborg, 413 46, Swed.
SOURCE: Infect. Immun. (1994), 62(10), 4339-46
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Enterotoxigenic Escherichia coli binds to enterocytes in the small intestine by means of antigenically distinct colonization factors (CFs), usually termed colonization factor antigens (CFAs), coli surface antigens (CS), or putative colonization factor antigens (PCFs). To explore the immunol. relationship between different CFs, the authors dissocd. **CFA/I** fimbriae into subunits and produced **monoclonal** antibodies (**MAbs**) against these subunits. They selected three **MAbs** that cross-reacted immunol. with a no. of different, whole purified CFs in a dot blot test and with the corresponding subunits in sodium dodecyl sulfate-polyacrylamide gel electrophoresis. One of the

MAbs, i.e., subunit **CFA/I** 17:8 (S-**CFA/I** 17:8), reacted more strongly with subunits of **CFA/I** than with whole purified fimbriae. This **MAb** cross-reacted with whole purified fimbriae and subunits of **CS4**, PCFO166, CS1, and CS2. Moreover, it bound strongly to a peptide of 25 amino acids corresponding to the N-terminal end of **CFA/I**. The other two **MAbs**, i.e., S-**CFA/I** 5:6 and S-**CFA/I** 8:11, cross-reacted with CS1, CS2, **CS4**, PCFO166, and CS17 fimbriae but reacted only slightly or not at all with the **CFA/I** peptide. **MAbs** S-**CFA/I** 17:8 and S-**CFA/I** 5:6 were shown to inhibit hemagglutination by bacterial strains that express either **CFA/I**, CS1, or **CS4**. In addn., the binding of enterotoxigenic E. coli strains expressing **CFA/I**, CS2, **CS4**, and PCFO166 to enterocyte-like cell-line Caco-2 was inhibited by both **MAbs**. These results show that several antigenically different CFs have common epitopes and that among these at least one is located in the N-terminal end of the subunit protein. Moreover, antibodies against the common epitopes seem to block binding of the bacterial strains that express different CFs to both erythrocytes and Caco-2 cells.

L6 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1993:166937 CAPLUS
DOCUMENT NUMBER: 118:166937
TITLE: Induction of colonization factor antigen I (**CFA/I**) and coli surface antigen 4 (**CS4**) of enterotoxigenic Escherichia coli: relevance for vaccine production
AUTHOR(S): Grewal, Harleen M. S.; Gaastra, Wim; Svennerholm, Ann Maria; Roeli, Jacob; Sommerfelt, Halvor
CORPORATE SOURCE: Cent. Int. Health, Univ. Bergen, Bergen, N-5021, Norway
SOURCE: Vaccine (1993), 11(2), 221-6
CODEN: VACCDE; ISSN: 0264-410X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Regulatory proteins control the expression of the fimbrial colonization factor antigens **CFA/I** and **CS4** of enterotoxigenic E. coli (ETEC). To examine the mechanism behind lack of expression of these antigens in spontaneous CFA-neg. mutants, the authors mobilized a recombinant plasmid harboring the cfaD gene, which encodes a pos. regulator of **CFA/I** and **CS4** expression, into such derivs. In electron microscopy, the induced surface structures were morphol. identical to the fimbriae of the **CFA/I**+

and **CS4+** wild type strains. Immunogold labeling with **monoclonal** antibodies showed that the distribution of **CFA/I** and **CS4** specific epitopes along the induced fimbriae was indistinguishable from that of the wild-type strains. The percentage of fimbriated cells was consistently higher in the cfaD transformants than in the corresponding wild type strains. The present work reports on the efficiency of the cloned cfaD gene in restoring and enhancing the prodn. of morphol. intact **CFA/I** and **CS4** fimbriae.

(FILE 'CAPLUS' ENTERED AT 15:52:08 ON 16 JUN 2000)

L7 262 SEA ABB=ON PLU=ON ((COLONIZ? OR COLONIS?)(W)FACTOR OR CFA)(3A)(1 OR I) OR CFAI OR CFA1
L8 1715 SEA ABB=ON PLU=ON CS4 OR (COLI SURFACE OR CS)(3A)4
L9 27 SEA ABB=ON PLU=ON L7 AND L8
L10 6 SEA ABB=ON PLU=ON L3 AND L9
L11 1 SEA ABB=ON PLU=ON L10 NOT L6
L12 0 SEA ABB=ON PLU=ON L10 NOT (L2 OR L6)

(FILE 'MEDLINE, BIOSIS, EMBASE, LIFESCI, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 16:07:44 ON 16 JUN 2000)

L13 36 S L10
L14 13 DUP REM L13 (23 DUPLICATES REMOVED)

L14 ANSWER 1 OF 13 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000085104 MEDLINE
DOCUMENT NUMBER: 20085104
TITLE: Prevalence of toxin types and colonization factors in enterotoxigenic Escherichia coli isolated during a 2-year period from diarrheal patients in Bangladesh.
AUTHOR: Qadri F; Das S K; Faruque A S; Fuchs G J; Albert M J; Sack R B; Svennerholm A M
CORPORATE SOURCE: International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka 1000, Bangladesh.. fqadri@icddrb.org
SOURCE: JOURNAL OF CLINICAL MICROBIOLOGY, (2000 Jan) 38 (1) 27-31.
Journal code: HSH. ISSN: 0095-1137.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY WEEK: 20000403
AB The prevalence of toxin types and colonization factors (CFs) of enterotoxigenic Escherichia coli (ETEC) was prospectively studied with fresh samples (n = 4,662) obtained from a 2% routine surveillance of diarrheal stool samples over 2 years, from September

1996 to August 1998. Stool samples were tested by enzyme-linked immunoassay techniques and with specific **monoclonal** antibodies for the toxins and CFs. The prevalence of ETEC was 14% (n = 662), with over 70% of the strains isolated from children 0 to 5 years of age, of whom 93% were in the 0- to 3-year-old age range. Of the total ETEC isolates, 49.4% were positive for the heat-stable toxin (ST), 25.4% were positive for the heat-labile toxin (LT) only, and 25.2% were positive for both LT and ST. The rate of ETEC isolation peaked in the hot summer months of May to September and decreased in winter. About 56% of the samples were positive for 1 or more of the 12 CFs that were screened for. The coli surface antigens **CS4**, CS5, and/or CS6 of the colonization factor antigen (CFA)/IV complex were most prevalent (incidence, 31%), followed by **CFA/I** (23.5%) and coli surface antigens CS1, CS2, and CS3 of CFA/II (21%). In addition, other CFs detected in decreasing order were CS7 (8%), CS14 (PCFO166) (7%), CS12 (PCFO159) (4%), CS17 (3%), and CS8 (CFA/III) (2.7%). The ST- or LT- and ST-positive ETEC isolates expressed the CFs known to be the most prevalent (**i**.e., **CFA/I**, **CFA** /II, and **CFA**/IV), while the strains positive for LT only did not. Among children who were infected with ETEC as the single pathogen, a trend of relatively more severe disease in children infected with ST-positive ($P < 0.001$) or LT- and ST-positive ($P < 0.001$) ETEC isolates compared to the severity of the disease in children infected with LT only-positive ETEC isolates was seen. This study supports the fact that ETEC is still a major cause of childhood diarrhea in Bangladesh, especially in children up to 3 years of age, and that measures to prevent such infections are needed in developing countries.

L14 ANSWER 2 OF 13 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 1999:38879 SCISEARCH
THE GENUINE ARTICLE: 151MW
TITLE: Oral, inactivated, whole cell enterotoxigenic Escherichia coli plus cholera toxin B subunit vaccine: Results of the initial evaluation in children
AUTHOR: Savarino S J (Reprint); Hall E R; Bassily S; Brown F M; Youssef F; Wierzba T F; Peruski L; ElMasry N A; Safwat M; Rao M; ElMohamady H; AbuElyazeed R; Naficy A; Svennerholm A M; Jertborn M; Lee Y J; Clemens J D
CORPORATE SOURCE: USN, RES PUBLICAT OFF, MED RES UNIT 3, PSC 452, BOX 5000, FPO, AE 09835 (Reprint); USN, MED RES UNIT 3, CAIRO, EGYPT; EGYPTIAN MINIST HLTH, BANHA, EGYPT; QALYUBIA GOVERNORATE, GOVERNORATE, EGYPT; NICHHD, DIV EPIDEMIOL STAT & PREVENT RES, NIH, BETHESDA, MD 20892; GOTHENBURG UNIV, DEPT MED MICROBIOL & IMMUNOL, S-41124 GOTHENBURG, SWEDEN
COUNTRY OF AUTHOR: USA; EGYPT; SWEDEN
Searcher : Shears 308-4994

SOURCE: JOURNAL OF INFECTIOUS DISEASES, (JAN 1999) Vol. 179, No. 1, pp. 107-114.
Publisher: UNIV CHICAGO PRESS, 5801 S ELLIS AVENUE, CHICAGO, IL 60637.
ISSN: 0022-1899.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 38

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Two randomized, double-blinded trials assessed the safety and immunogenicity of an oral, killed enterotoxigenic Escherichia coli (ETEC) plus cholera toxin B subunit vaccine in Egyptian children. Two doses of vaccine or E. coli K-12 were given 2 weeks apart to 105 6- to 12-year-olds and 97 2- to 5-year-olds. Safety was monitored for 3 days after each dose. Blood was collected before immunization and 7 days after each dose to measure immune responses. Few children reported postdosing symptoms, with no differences in the frequency of symptoms between treatment groups. Most vaccinees had an IgA antibody-secreting cell response against **colonization factor** antigen I(100%, 6-12 years; 95%, 2-5 years), coli surface antigen 2 (92%, 6-12 years; 83%, 2-5 years), and **coli surface** antigen **4** (93%, 6-12 years). Vaccination evoked a greater than or equal to 4-fold rise in antitoxic IgA and IgG titers in 93% and 81% of children, respectively, In conclusion, the oral ETEC vaccine was safe and immunogenic in 2- to 12-year-old children, justifying further evaluation in infants.

L14 ANSWER 3 OF 13 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1998-145553 [13] WPIDS
DOC. NO. NON-CPI: N1998-115141
DOC. NO. CPI: C1998-047618

TITLE: **Monoclonal** antibody agglutinating Escherichia coli with **CS4-CFA/I** family protein - is useful in assays and for treatment or prophylaxis against illness arising from infection with E. coli bearing **CS4-CFA/I** family proteins.

DERWENT CLASS: B04 D16 S03
INVENTOR(S): CASSELS, F; LEES, A; SCHUMAN, R
PATENT ASSIGNEE(S): (USSA) US DEPT OF THE ARMY; (VIRI-N) VIRION SYSTEMS INC
COUNTRY COUNT: 20
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 9805687 A1 19980212 (199813)* EN 14
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP
EP 918796 A1 19990602 (199926) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9805687	A1	WO 1997-US13477	19970801
EP 918796	A1	EP 1997-938077	19970801
		WO 1997-US13477	19970801

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 918796	A1	Based on	WO 9805687

PRIORITY APPLN. INFO: US 1996-23075 19960802
AN 1998-145553 [13] WPIDS
AB WO 9805687 A UPAB: 19980330
New **monoclonal** antibody binds exclusively and specifically to sequence (I), agglutinates bacteria bearing **CS4-CFA/I** family proteins and is produced by **hybridoma 96-109FE8** IH11.SAVALTYS (I).

USE - The **monoclonal** antibody can agglutinate members of the Escherichia coli family CSA-**CFA/I** , since it was raised to a consensus peptide (sequence (II)) known to raise antibodies against proteins of all the CSA-**CFA/I** family. E. coli causing diarrhoea are grouped into five classes, of which enterotoxigenic (ETEC), to which the **CS4-CFA /I** family belong, are the most common and pose the greatest risk to travellers. ETEC E. coli cause high infant mortality and illness in adult travellers in developing countries. The antibody is useful in assays (kits provided; not claimed) to detect/identify organisms bearing **CS4**-CFA family proteins, by contacting cultures of organisms for sufficient time for interaction, and determining whether a **CS4-CFA/ I** family protein/antibody complex has formed (claimed). It can be included in compositions with a carrier appropriate for application to bacteria-containing growth media, optionally with a tag e.g. a fluorescing agent or colorometric tag, to assist identification of the complex (claimed). It can also be included in compositions with pharmaceutically acceptable carriers, especially saline (claimed), useful for treating or prophylaxing against illness arising from infection with bacteria bearing **CS4-CFA/I** family proteins (claimed).

Searcher : Shears 308-4994

VEKNITVTASVDPTIDLLQADGSALPSAVALTYSPA (II)

ADVANTAGE - Bacterial cultures of several ETEC strains were not agglutinated at 1 mu g antibody/ml **hybridoma** tissue culture supernatant, whilst at 20-fold concentration **CFA/I** expressing strain was agglutinated and at 130-fold concentration all strains were agglutinated.

Dwg.0/0

L14 ANSWER 4 OF 13 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 1998418525 MEDLINE

DOCUMENT NUMBER: 98418525

TITLE: Epidemiology and properties of heat-stable enterotoxin-producing Escherichia coli serotype O169:H41.

AUTHOR: Nishikawa Y; Helander A; Ogasawara J; Moyer N P; Hanaoka M; Hase A; Yasukawa A

CORPORATE SOURCE: Department of Epidemiology, Osaka City Institute of Public Health and Environmental Sciences, Tennoji, Osaka, Japan.

SOURCE: EPIDEMIOLOGY AND INFECTION, (1998 Aug) 121 (1) 31-42. Journal code: EPI. ISSN: 0950-2688.

PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199812

ENTRY WEEK: 19981201

AB Enterotoxigenic Escherichia coli (ETEC) serotype O169:H41 organisms have become the most prevalent ETEC in Japan since the first outbreak in 1991. It was assumed that the outbreaks were due to clonal spread of this new ETEC serotype. The relationship of 32 strains isolated from 6 outbreaks were examined for biotype, antibiotic susceptibility, enterotoxigenicity, protein banding pattern, lipopolysaccharide banding pattern, plasmid analysis, and ribotyping. Further, the strains were examined by haemagglutination, surface hydrophobicity, and the ability to adhere to HEp-2 cells. The present study suggests that the outbreaks were caused by multiple clones of STp-producing O169:H41 since they showed differences in ribotype and outer membrane protein banding patterns. The strains did not agglutinate human or bovine red blood cells in a mannose-resistant manner. They adhered to HEp-2 cells in a manner resembling enteroaggregative E. coli. Five strains were examined by dot-blot tests for the **colonization factor** antigens **CFA/I**, CS1, CS2, CS3, **CS4**, CS5, CS6, CS7, PCFO159, PCFO166 and CFA/III. Although four strains expressed CS6, no structure for CS6 was identified. A strain that the anti-CS6 **MAbs** did not react with could adhere to HEp-2 cells in mannose resistant manner; thus, it is unlikely that CS6 play an important role in the adhesion to the cells. Electron

microscopy studies of the O169:H41 strains suggested that curly fimbriae, a possible new colonization factor, may be playing an important role in the adhesion of the bacteria to HEp-2 cells. In conclusion, outbreaks due to ETEC O169:H41 were caused by multiple clones, and the strains should be examined in detail for a possible new colonization factor.

L14 ANSWER 5 OF 13 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 97:114496 SCISEARCH
THE GENUINE ARTICLE: WE900
TITLE: A new putative fimbrial colonization factor, CS19, of human enterotoxigenic Escherichia coli
AUTHOR: Grewal H M S; Valvatne H; Bhan M K; vanDijk L; Gaastra W; Sommerfelt H (Reprint)
CORPORATE SOURCE: UNIV BERGEN, CTR INT HLTH, ARMAUER HANSENS BLDG, N-5021 BERGEN, NORWAY (Reprint); UNIV BERGEN, CTR INT HLTH, N-5021 BERGEN, NORWAY; UNIV BERGEN, BIOTECHNOL LAB, N-5021 BERGEN, NORWAY; UNIV BERGEN, DEPT MICROBIOL & IMMUNOL, GADES INST, N-5021 BERGEN, NORWAY; ALL INDIA INST MED SCI, DEPT PEDIAT, DIV GASTROENTEROL & ENTER INFECT, NEW DELHI, INDIA; UNIV UTRECHT, FAC VET MED, INST INFECT DIS & IMMUNOL, UTRECHT, NETHERLANDS
COUNTRY OF AUTHOR: NORWAY; INDIA; NETHERLANDS
SOURCE: INFECTION AND IMMUNITY, (FEB 1997) Vol. 65, No. 2, pp. 507-513.
Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171.
ISSN: 0019-9567.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 54
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A gene probe derived from the **colonization factor** antigen I (**CFA/I**) operon cross-hybridized at very low stringency to plasmid DNA from coli surface antigen 17 (CS17)-producing enterotoxigenic Escherichia coli (ETEC) and from the ETEC strain F595C, which was negative for previously described CFAs, CSs, and putative colonization factors (PCFs). A 16-kDa protein was identified in sodium dodecyl sulfate-polyacrylamide gel electrophoresis of heat extracts prepared after growth of strain F595C at 37 degrees C on CFA agar containing bile salts. Transmission electron microscopy revealed bile salt- and temperature-dependent expression of fimbriae with a diameter of 7 nm. After transformation with a recombinant plasmid harboring the cfaR gene, which encodes a positive regulator of several CFAs, PCFs, and CSs, the 16-kDa protein was hyperexpressed. Polyclonal antibodies raised against this protein bound to the fimbriae and

inhibited the adhesion of F595C bacteria to tissue-cultured Caco-2 cells. Nucleotide sequence determination of the gene encoding the 16-kDa fimbrial subunit revealed a high degree of amino acid sequence homology to the **CFA/I**, CS1, CS2, **CS4**, CS14, and CS17 polypeptides. The term CS19 is proposed for the new fimbria.

L14 ANSWER 6 OF 13 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 1998:42748 SCISEARCH
THE GENUINE ARTICLE: YN990
TITLE: Infection with **colonization factor** antigen **I**-expressing enterotoxigenic Escherichia coli boosts antibody responses against heterologous colonization factors in primed subjects
AUTHOR: Rudin A (Reprint); Wiklund G; Wenneras C; Qadri F
CORPORATE SOURCE: GOTHENBURG UNIV, DEPT MED MICROBIOL & IMMUNOL, GULDHEDSGATAN 10A, S-41346 GOTHENBURG, SWEDEN (Reprint); INT CTR DIARRHOEAL DIS RES, DHAKA, BANGLADESH
COUNTRY OF AUTHOR: SWEDEN; BANGLADESH
SOURCE: EPIDEMIOLOGY AND INFECTION, (DEC 1997) Vol. 119, No. 3, pp. 391-393.
Publisher: CAMBRIDGE UNIV PRESS, 40 WEST 20TH STREET, NEW YORK, NY 10011-4211.
ISSN: 0950-2688.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 11
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Enterotoxigenic Escherichia coli (ETEC) adhere to the intestinal mucosa by a number of fimbrial colonization factors (CFs) that have been claimed to induce only type-specific immunity. However, adult Bangladeshi patients infected with **CFA/I**-expressing bacteria, developed significant plasma IgA antibody responses, as determined by enzyme-linked immunosorbent assay, not only against the homologous fimbriae but also against several heterologous CFs, i.e. CS1, CS2, **CS4** and PCFO166 fimbriae. In contrast, North American volunteers, who had probably not been infected by ETEC previously, responded With serum IgA against **CFA/I** fimbriae but not against any other CFs after symptomatic infection with **CFA/I**-expressing ETEC. Thus, infection with **CFA/I**-expressing bacteria may boost immune responses against CFs with a related amino acid sequence in previously primed subjects.

L14 ANSWER 7 OF 13 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 96425254 MEDLINE
DOCUMENT NUMBER: 96425254

TITLE: **Monoclonal** antibodies against fimbrial subunits of **colonization factor** antigen **I** (**CFA/I**) inhibit binding to human enterocytes and protect against enterotoxigenic Escherichia coli expressing heterologous colonization factors.

AUTHOR: Rudin A; Olbe L; Svennerholm A M
CORPORATE SOURCE: Department of Medical Microbiology and Immunology, Goteborg University, Sweden.

SOURCE: MICROBIAL PATHOGENESIS, (1996 Jul) 21 (1) 35-45. Journal code: MIC. ISSN: 0882-4010.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY WEEK: 19970204

AB Enterotoxigenic Escherichia coli (ETEC) bind to enterocytes in the small intestine by means of antigenically distinct colonization factors (CFs). By immunizing with isolated subunits of **CFA /I** fimbriae we have previously produced **monoclonal** antibodies (**MAbs**) that cross-react immunologically in vitro with several CFs. Two of these **MAbs** [S(subunit)-**CFA/ I** 17:8 and S-**CFA/I** 5:6] were found to significantly inhibit the binding of ETEC strains expressing either homologous or heterologous CFs, **i**.e. **CFA/I** and **CS4**, to isolated human jejunal enterocytes. The two **MAbs** also conferred passive protection against fluid accumulation in rabbit ileal loops caused by **CFA/I**-as well as **CS4**-expressing ETEC strains. Immunoelectron microscopy studies showed that both **MAbs** bound specifically to **CFA/I** as well as to **CS4** fimbriae expressed on bacteria. These results indicate the possibility to induce anti-CF antibodies that can protect against ETEC infection caused by bacteria expressing not only homologous but also heterologous CFs, by immunizing with fimbrial subunits.

L14 ANSWER 8 OF 13 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 95012620 MEDLINE
DOCUMENT NUMBER: 95012620
TITLE: **Monoclonal** antibodies against enterotoxigenic Escherichia coli **colonization factor** antigen **I** (**CFA/ I**) that cross-react immunologically with heterologous CFAs.

AUTHOR: Rudin A; McConnell M M; Svennerholm A M
CORPORATE SOURCE: Department of Medical Microbiology and Immunology, University of Goteborg, Sweden.

SOURCE: INFECTION AND IMMUNITY, (1994 Oct) 62 (10) 4339-46.
Journal code: GO7. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199501

AB Enterotoxigenic Escherichia coli binds to enterocytes in the small intestine by means of antigenically distinct colonization factors (CFs), usually termed colonization factor antigens (CFAs), coli surface antigens (CS), or putative colonization factor antigens (PCFs). To explore the immunological relationship between different CFs, we dissociated **CFA/I** fimbriae into subunits and produced **monoclonal** antibodies (**MAbs**) against these subunits. We selected three **MAbs** that cross-reacted immunologically with a number of different, whole purified CFs in a dot blot test and with the corresponding subunits in sodium dodecyl sulfate-polyacrylamide gel electrophoresis. One of the **MAbs**, i.e., subunit **CFA/I** 17:8 (S-**CFA/I** 17:8), reacted more strongly with subunits of **CFA/I** than with whole purified fimbriae. This **MAb** cross-reacted with whole purified fimbriae and subunits of **CS4**, PCFO166, CS1, and CS2. Moreover, it bound strongly to a peptide of 25 amino acids corresponding to the N-terminal end of **CFA/I**. The other two **MAbs**, i.e., S-**CFA/I** 5:6 and S-**CFA/I** 8:11, cross-reacted with CS1, CS2, **CS4**, PCFO166, and CS17 fimbriae but reacted only slightly or not at all with the **CFA/I** peptide. **MAbs** S-**CFA/I** 17:8 and S-**CFA/I** 5:6 were shown to inhibit hemagglutination by bacterial strains that express either **CFA/I**, CS1, or **CS4**. In addition, the binding of enterotoxigenic E. coli strains expressing **CFA/I**, CS2, **CS4**, and PCFO166 to enterocyte-like cell-line Caco-2 was inhibited by both **MAbs**. These results show that several antigenically different CFs have common epitopes and that among these at least one is located in the N-terminal end of the subunit protein. Moreover, antibodies against the common epitopes seem to block binding of the bacterial strains that express different CFs to both erythrocytes and Caco-2 cells.

L14 ANSWER 9 OF 13 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 94:321889 SCISEARCH
THE GENUINE ARTICLE: NM112
TITLE: COLONIZATION FACTOR ANTIGENS (CFAS) OF ENTEROTOXIGENIC ESCHERICHIA-COLI CAN PRIME AND BOOST IMMUNE-RESPONSES AGAINST HETEROLOGOUS CFAS
AUTHOR: RUDIN A; SVENNERHOLM A M (Reprint)

CORPORATE SOURCE: GOTHENBURG UNIV, DEPT MED MICROBIOL & IMMUNOL, GULDHEDSGATAN 10 A, S-41346 GOTHENBURG, SWEDEN (Reprint); GOTHENBURG UNIV, DEPT MED MICROBIOL & IMMUNOL, S-41346 GOTHENBURG, SWEDEN
COUNTRY OF AUTHOR: SWEDEN
SOURCE: MICROBIAL PATHOGENESIS, (FEB 1994) Vol. 16, No. 2, pp. 131-139.
ISSN: 0882-4010.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 31

L14 ANSWER 10 OF 13 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 93175124 MEDLINE
DOCUMENT NUMBER: 93175124
TITLE: Induction of **colonization factor** antigen **I** (**CFA/I**) and **coli surface** antigen **4** (**CS4**) of enterotoxigenic Escherichia coli: relevance for vaccine production.
AUTHOR: Grewal H M; Gaastra W; Svennerholm A M; Roli J; Sommerfelt H
CORPORATE SOURCE: Centre for International Health, University of Bergen, Haukeland Hospital, Norway..
SOURCE: VACCINE, (1993) 11 (2) 221-6.
Journal code: X6O. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199305
AB Regulatory proteins control the expression of the fimbrial **colonization factor** antigens **CFA/I** and **CS4** of enterotoxigenic Escherichia coli (ETEC). To examine the mechanism behind lack of expression of these antigens in spontaneous CFA-negative mutants, we mobilized a recombinant plasmid harbouring the cfaD gene, which encodes a positive regulator of **CFA/I** and **CS4** expression, into such derivatives. In electron microscopy, the induced surface structures were morphologically identical to the fimbriae of the **CFA/I**+ and **CS4**+ wild type strains. Immunogold labelling with **monoclonal** antibodies showed that the distribution of **CFA/I** and **CS4** specific epitopes along the induced fimbriae was indistinguishable from that of the wild type strains. The percentage of fimbriated cells was consistently higher in the cfaD transformants than in the corresponding wild type strains. The present work reports on the efficiency of the cloned cfaD gene in

restoring and enhancing the production of morphologically intact **CFA/I** and **CS4** fimbriae.

L14 ANSWER 11 OF 13 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 92:507953 SCISEARCH
THE GENUINE ARTICLE: JJ861
TITLE: GENETIC-RELATIONSHIP OF PUTATIVE COLONIZATION FACTOR-O166 TO **COLONIZATION FACTOR** ANTIGEN-**I** AND **COLI** **SURFACE** ANTIGEN-**4** OF ENTEROTOXIGENIC ESCHERICHIA-COLI
AUTHOR: SOMMERFELT H (Reprint); GREWAL H M S; SVENNERHOLM A M; GAASTRA W; FLOOD P R; VIBOUD G; BHAN M K
CORPORATE SOURCE: UNIV BERGEN, HAUKELAND HOSP, CTR INT HLTH, N-5021 BERGEN, NORWAY (Reprint); UNIV BERGEN, BERGEN HIGH TECHNOL CTR, CTR BIOTECHNOL, N-5020 BERGEN, NORWAY; UNIV BERGEN, INST ANAT, N-5009 BERGEN, NORWAY; ALL INDIA INST MED SCI, DEPT PEDIAT, DIV GASTROENTEROL & ENTER INFECT, NEW DELHI 110029, INDIA; GOTHENBURG UNIV, DEPT MED MICROBIOL & IMMUNOL, S-41346 GOTHENBURG, SWEDEN; UNIV UTRECHT, FAC VET MED, INST INFECT DIS & IMMUNOL, 3508 TD UTRECHT, NETHERLANDS
COUNTRY OF AUTHOR: NORWAY; INDIA; SWEDEN; NETHERLANDS
SOURCE: INFECTION AND IMMUNITY, (SEP 1992) Vol. 60, No. 9, pp. 3799-3806.
ISSN: 0019-9567.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 50
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Plasmid DNA from two strains of enterotoxigenic Escherichia coli harboring genes encoding **coli surface** antigen **4** (**CS4**) and from seven Indian enterotoxigenic E. coli isolates cross-hybridized at low stringency but not at high stringency with two polynucleotide probes derived from the **colonization factor** antigen **I** (**CFA/I**) operon. Low-stringency Southern blot hybridization of PstI-digested plasmid DNA from the seven Indian isolates yielded characteristic restriction fragment patterns, distinct from those of **CS4**- and **CFA/I** -associated plasmid DNA. Two of the Indian strains were transformed with a recombinant plasmid harboring the cfaD gene, which encodes a positive regulator of **CFA/I** and **CS4** genes. The cfaD transformants produced large amounts of putative colonization factor O166 (PCFO166) irrespective of whether the nutrient agar contained bile salts, a growth factor otherwise required for adequate PCFO166 expression. A considerable interstrain variation in the level of PCFO166 production could be explained by

differences in the proportion of bacteria that were fimbriated, as visualized by electron microscopy. The N-terminal amino acid sequence of PCFO166 fimbrial protein showed a high degree of homology with the corresponding sequences of **CFA/I** and **CS4**.

L14 ANSWER 12 OF 13 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 92:379017 SCISEARCH
THE GENUINE ARTICLE: HZ759
TITLE: USE OF NONRADIOACTIVE DNA HYBRIDIZATION FOR IDENTIFICATION OF ENTEROTOXIGENIC ESCHERICHIA-COLI HARBORING GENES FOR **COLONIZATION FACTOR** ANTIGEN-**I**, **COLI SURFACE** ANTIGEN-**4**, OR PUTATIVE COLONIZATION FACTOR-O166
AUTHOR: SOMMERFELT H (Reprint); GREWAL H M S; GAASTRA W; SVENNERHOLM A M; BHAN M K
CORPORATE SOURCE: UNIV BERGEN, HAUKELAND HOSP, CTR INT HLTH, N-5021 BERGEN, NORWAY (Reprint); UNIV BERGEN, HAUKELAND HOSP, DEPT MED B, N-5021 BERGEN, NORWAY; UNIV BERGEN, CTR BIOTECHNOL, N-5020 BERGEN, NORWAY; UNIV UTRECHT, FAC VET MED, INST INFECT DIS & IMMUNOL, 3508 TD UTRECHT, NETHERLANDS; GOTHENBURG UNIV, DEPT MED MICROBIOL & IMMUNOL, S-41346 GOTHENBURG, SWEDEN; ALL INDIA INST MED SCI, DEPT PEDIAT, DIV GASTROENTEROL & ENTER INFECT, NEW DELHI 110029, INDIA
COUNTRY OF AUTHOR: NORWAY; NETHERLANDS; SWEDEN; INDIA
SOURCE: JOURNAL OF CLINICAL MICROBIOLOGY, (JUL 1992) Vol. 30, No. 7, pp. 1823-1828.
ISSN: 0095-1137.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: 43
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We developed an accurate nonradioactive colony hybridization assay (NCHA) using a digoxigenin-labeled polynucleotide probe and an antidigoxigenin alkaline phosphatase conjugate for the identification of enterotoxigenic Escherichia coli (ETEC) harboring genes for **colonization factor** antigen **I** (**CFA/I**), **coli surface** antigen **4** (**CS4**), or putative colonization factor O166 (PCFO166). In this 2-day assay, visual registration of color intensity could be used to distinguish between **CFA/I**-positive strains and strains with the genetic potential to express **CS4** or PCFO166. A rapid NCHA was developed by which the results could be read visually 7 h and 45 min after inoculation of the bacteria. In the rapid NCHA, densitometry

verified the visual discrimination between four groups of E. coli; ETEC with the **CFA/I** gene, ETEC with the **CS4** gene, ETEC with the PCFO 1 66 gene, and E. coli strains that lack such genes. As a confirmatory test, plasmids from ETEC with the **CFA/I**, **CS4**, or PCFO166 gene were differentiated by their characteristic restriction fragment patterns in nonradioactive Southern blot hybridization.

L14 ANSWER 13 OF 13 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 92129593 MEDLINE
DOCUMENT NUMBER: 92129593
TITLE: Colonization factors of enterotoxigenic Escherichia coli isolated from children with diarrhea in Argentina.
AUTHOR: Binsztein N; Jouve M J; Viboud G I; Lopez Moral L; Rivas M; Orskov I; Ahren C; Svennerholm A M
CORPORATE SOURCE: Instituto Nacional de Microbiologia Carlos G. Malbran, Buenos Aires, Argentina..
SOURCE: JOURNAL OF CLINICAL MICROBIOLOGY, (1991 Sep) 29 (9) 1893-8.
Journal code: HSH. ISSN: 0095-1137.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205

AB A prospective study was performed to evaluate the presence of colonization factor antigens (CFAs) in enterotoxigenic Escherichia coli (ETEC) strains isolated from 1,211 children with diarrhea in Argentina. One hundred nine ETEC strains that were isolated from seven different laboratories in various regions of the country were tested for CFAs by using **monoclonal** antibodies against **CFA/I** and E. coli surface antigens CS1, CS2, and CS3 of CFA/II and **CS4** and CS5 of CFA/IV; a polyclonal antiserum against CS6 was used. The CFAs searched for were found in 52% of the ETEC strains: 23% of the strains carried **CFA/I**, 17% carried **CFA**/IV, and 12% carried CFA/II. All of the **CFA/I** strains produced heat-stable enterotoxin, and several of them were of the prevalent serotypes O153:H45 and O78:H12. Among the 19 strains expressing CFA/IV, 16 expressed CS5 and CS6 and produced the heat-stable enterotoxin and most were of serotype O128:H21; the remaining 3 strains produced CS6 only. No ETEC strains expressing **CS4** were found. Most (11 of 13) of the CFA/II-carrying ETEC strains expressed CS1 and CS3, and 10 of them were of the O6:K15:H16 serotype and produced both heat-labile and heat-stable toxins. As many as 24 of the 109 CFA-negative ETEC strains gave mannose-resistant hemagglutination with erythrocytes from different species; 4 strains had high surface hydrophobicity, suggesting the presence of additional, as yet

undefined, colonization factors in up to 25% of the ETEC isolates.

(FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, LIFESCI, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 16:17:41 ON 16 JUN 2000)

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L15         162 S CASSELS F?/AU
L16        2725 S LEES A?/AU                    - Author(s)
L17         139 S SCHUMAN R?/AU
L18           2 S L15 AND L16 AND L17
L19           9 S L15 AND (L16 OR L17)
L20           8 S L16 AND L17
L21          94 S (L15 OR L16 OR L17) AND L3
L22           8 S L21 AND L7
L23          21 S L18 OR L19 OR L20 OR L22
L24           6 DUP REM L23 (15 DUPLICATES REMOVED)
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L24 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 1

ACCESSION NUMBER: 2000:75872 CAPLUS

TITLE: Activation of soluble polysaccharides with 1-cyano-4-dimethylaminopyridinium tetrafluoroborate (CDAP) for use in protein-polysaccharide conjugate vaccines and immunological reagents. II. Selective crosslinking of proteins to CDAP-activated polysaccharides

AUTHOR(S): Shafer, Douglas E.; Toll, Barbara; **Schuman, Richard F.**; Nelson, Brett L.; Mond, James J.; **Lees, Andrew**

CORPORATE SOURCE: Virion Systems, Inc., Rockville, MD, 20850, USA

SOURCE: Vaccine (2000), 18(13), 1273-1281
CODEN: VACCDE; ISSN: 0264-410X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Covalently linking protein to polysaccharides converts the anti-polysaccharide immune response from a T-cell independent response to one which is T-cell dependent. The org. cyanylating reagent 1-cyano-4-dimethylaminopyridinium tetrafluoroborate (CDAP) has been used to activate polysaccharides, which can then be reacted with spacer reagents or directly with protein. We wished to explore ways in which proteins could be linked to CDAP-activated polysaccharides to conjugate in a more controlled and selective fashion. To this end, we examd. the reaction of nucleophilic amino acids with CDAP-activated polysaccharides under basic and acidic conditions. We found that lysine, cysteine and histidine but not methionine, serine or tyrosine conjugated to CDAP-activated dextran. We also examd. the reaction of various spacer reagents with CDAP-activated dextran as a function of pH. The addn. of hexanediamine was highly pH dependent and maximal at pH 9.3. In contrast, the addn. of adipic dihydrazide, which has a pKa of ca 2.5

was essentially independent of pH. By performing the conjugation reaction at pH 5, we were able to selectively couple hydrazides even in the presence of high concns. of amines. Proteins derivatized with limited nos. of hydrazides could be conjugated to CDAP-activated polysaccharides at pH5, where the native protein was not reactive. Proteins could be derivatized with hydrazides on carboxyls using adipic dihydrazide and a water sol. carbodiimide or on amines using a mild two-step reaction. Tetanus toxoid-pneumococcal type 14 conjugates produced by coupling hydrazide-derivatized tetanus toxoid under acidic conditions induced anti-polysaccharide antibodies at titers comparable to that stimulated by conjugates produced using a basic coupling pH. Our data suggest that crosslinking was occurring only with the limited no. of hydrazides on the protein and that we achieved limited and selective crosslinking between the protein and CDAP-activated polysaccharide. This work also demonstrates that CDAP-mediated conjugation to polysaccharides can be applied even to very pH sensitive proteins and polysaccharides.

REFERENCE COUNT: 19

REFERENCE(S):
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(2) Bernatowicz, M; Anal Biochem 1986, V155, P95 CAPLUS
(5) Heimgartner, U; Biochem J 1990, V267, P585 CAPLUS
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(8) Jensen, K; Acta Chem Scand 1966, V20, P2091 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 2

ACCESSION NUMBER: 1999:486635 CAPLUS

DOCUMENT NUMBER: 131:225892

TITLE: Characterization of an enterotoxigenic Escherichia coli strain from Africa expressing a putative colonization factor

AUTHOR(S): Khalil, Sami B.; **Cassels, Frederick J.**; Shaheen, Hind I.; Pannell, Lewis K.; El-Ghorab, Nemat; Kamal, Karim; Mansour, Moustafa; Savarino, Stephen J.; Peruski, Leonard F., Jr.

CORPORATE SOURCE: Research Sciences Department, U.S. Naval Medical Research Unit No. 3, Cairo, Egypt

SOURCE: Infect. Immun. (1999), 67(8), 4019-4026
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An enterotoxigenic Escherichia coli (ETEC) strain of serotype

O114:H- that expressed both heat-labile and heat-stable enterotoxins and tested neg. for colonization factors (CF) was isolated from a child with diarrhea in Egypt. This strain, WS0115A, induced hemagglutination of bovine erythrocytes and adhered to the enterocyte-like cell line Caco-2, suggesting that it may elaborate novel fimbriae. Surface-expressed antigen purified by differential ammonium sulfate pptn. and column chromatog. yielded a single protein band with Mr 14,800 when resolved by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (16% polyacrylamide). A **monoclonal** antibody against this putative fimbrial antigen was generated and reacted with strain WS0115A and also with CS1-, CS17-, and CS19-pos. strains in a dot blot assay. Reactivity was temp. dependent, with cells displaying reactivity when grown at 37.degree.C but not when grown at 22.degree.C. Immunoblot anal. of a fimbrial prepn. from strain WS0115A showed that the **monoclonal** antibody reacted with a single protein band. Electron microscopy and immunoelectron microscopy revealed fimbria-like structures on the surface of strain WS0115A. These structures were rigid and measured 6.8 to 7.4 nm in diam. Electrospray mass-spectrometric anal. showed that the mass of the purified fimbria was 14,965 Da. The N-terminal sequence of the fimbria established that it was a member of the **CFA/I** family, with sequence identity to the amino terminus of CS19, a new CF recently identified in India. Cumulatively, our results suggest that this fimbria is CS19. Screening of a collection of ETEC strains isolated from children with diarrhea in Egypt found that 4.2% of strains originally reported as CF neg. were pos. for this CF, suggesting that it is biol. relevant in the pathogenesis of ETEC.

REFERENCE COUNT: 46

REFERENCE(S):
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(5) Cassels, F; Infect Immun 1992, V60, P2174 CAPLUS
(6) Cassels, F; J Ind Microbiol 1995, V15, P214 CAPLUS
(9) Chait, B; Science 1992, V257, P1885 CAPLUS
(11) Darfeuille-Michaud, A; Infect Immun 1986, V52, P468 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 3

ACCESSION NUMBER: 1998:112385 CAPLUS

DOCUMENT NUMBER: 128:166363

TITLE: **Monoclonal** antibody which agglutinates Escherichia coli having the CS4-**CFA/I** family protein

INVENTOR(S): **Cassels, Frederick; Lees, Andrew; Schuman, Richard**

Searcher : Shears 308-4994

PATENT ASSIGNEE(S): United States Dept. of the Army, USA; Virion Systems Inc.
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9805687	A1	19980212	WO 1997-US13477	19970801
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 918796	A1	19990602	EP 1997-938077	19970801
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1996-23075 19960802
WO 1997-US13477 19970801

AB A **monoclonal** antibody to a consensus peptide of the formula: VEKNITVTASVDPTIDLLQADGSALPSAVALTYSPA. The **monoclonal** antibody of the invention binds exclusively to the sequence SAVALTYS and has use as a diagnostic and for prophylaxis against illness arising from enterotoxigenic E. coli which produces CS4-**CFA/I** family of proteins and for treatment of disease arising therefrom.

L24 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:459893 CAPLUS
DOCUMENT NUMBER: 127:148145
TITLE: Antibody to N-terminal consensus peptide is cross-reactive with all six members of the enterotoxigenic E. coli CFA/I family
AUTHOR(S): **Cassels, F. J.; Lees, A.**; Hansen, B. D.; Barringer, J. D.; Nelson, B. L.; Ryu, H.
CORPORATE SOURCE: Department of Gastroenterology, Walter Reed Army Institute of Research, Washington, DC, 20307, USA
SOURCE: Cytokines, Cholera Gut, [Pap. Jt. Meet. U. S.-Jpn. Coop. Med. Sci. Program Panels Malnutr. Cholera] (1997), Meeting Date 1995, 275-279. Editor(s): Keusch, Gerald T.; Kawakami, Masanobu. IOS Press: Amsterdam, Neth.
CODEN: 64SIAE
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The CFA/I family of enterotoxigenic Escherichia coli (ETEC)

colonization factors (CF) consists of CFA/I, CS1, CS2, CS4, CS17, and PCF 0166. They have been grouped as a family due to protein sequence homol. as well as immunol. cross-reactivity. In this study, addnl. protein sequence of CS2, CS4, CS17, and PCF 0166 was obtained. From this sequence a consensus was derived, a thirty-six amino acid peptide corresponding to this consensus synthesized, the peptide conjugated to a carrier protein, and rabbits immunized. Sera tested pos. in an immunoblot (Western) assay against the peptide as well as against each of the members of the CFA/I family. The sera also agglutinated ETEC strains bearing CS1, CS2, and CFA/I in a slide agglutination test. These data demonstrate that a peptide derived from the consensus of the N-terminus of the CFA/I family is immunogenic and cross-reactive to each member of the family. It is hoped that these and addnl. studies may lead to a cross-protective vaccine to ETEC strains bearing these CF, as well as to a broadly reactive reagent useful in CF detection.

L24 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 4
ACCESSION NUMBER: 1997:559889 CAPLUS
DOCUMENT NUMBER: 127:246818
TITLE: Linear epitopes of colonization factor antigen I and peptide vaccine approach to enterotoxigenic Escherichia coli
AUTHOR(S): **Cassels, Fj**; Jarboe, Dl; Reid, Rh; **Lees, A.**; Deal, Cd
CORPORATE SOURCE: Department of Gastroenterology, Washington, DC, 20307, USA
SOURCE: J. Ind. Microbiol. Biotechnol. (1997), 19(1), 66-70
CODEN: JIMBFL; ISSN: 1367-5435
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Enterotoxigenic Escherichia coli (ETEC) cause diarrhea in infants and in travelers to developing countries. The bacteria utilize colonization factors (CF) for adherence to intestinal epithelia, then release toxins causing diarrhea. CF are strong immunogens as well as protective antigens. While 20 ETEC CF have been described in the literature, 11 CF are prominent enough to be considered for vaccine targeting. Of this group, six of the members fall into the CFA/I family of CF. Geysen pin (peptide) linear epitope anal. demonstrated that three regions contg. linear epitopes exist in CFA/I, and that both B- and T-cell linear epitopes of CFA/I were concd. at the N-terminus of the protein. The authors have detd. N-terminal sequence of the CFA/I family members not previously sequenced. Comparison of the protein sequence of the six members of the family showed a strong homol. up to residue 36. A peptide of 36 amino acids representing a consensus of the six sequences was synthesized and used to immunize animals. The antibody induced to

the peptide was reactive to the peptide as well as cross-reactive to each member of the CFA/I family in Western blots. In addn., this antibody agglutinated three of the six members of the CFA/I family when added to whole cells expressing the native CF. The authors are currently evaluating different carriers and conjugation methods to maximize prodn. of high titer, agglutinating antibody. It is hoped that this and related research will result in an effective and inexpensive cross-reactive and cross-protective ETEC vaccine.

L24 ANSWER 6 OF 6 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 92:353949 SCISEARCH
THE GENUINE ARTICLE: HX421
TITLE: ANALYSIS OF ESCHERICHIA-COLI **COLONIZATION FACTOR** ANTIGEN-I LINEAR B-CELL EPITOPES, AS DETERMINED BY PRIMATE RESPONSES, FOLLOWING PROTEIN-SEQUENCE VERIFICATION
AUTHOR: **CASSELS F J (Reprint)**; DEAL C D; REID R H; JARBOE D L; NAUSS J L; CARTER J M; BOEDEKER E C
CORPORATE SOURCE: WALTER REED ARMY MED CTR, DEPT GASTROENTEROL, WASHINGTON, DC, 20307 (Reprint); WALTER REED ARMY MED CTR, DEPT BACTERIAL DIS, WASHINGTON, DC, 20307
COUNTRY OF AUTHOR: USA
SOURCE: INFECTION AND IMMUNITY, (JUN 1992) Vol. 60, No. 6, pp. 2174-2181.
ISSN: 0019-9567.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 45
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Colonization factor** antigen **I** (**CFA/I**)-bearing strains of enterotoxigenic Escherichia coli (ETEC) are responsible for a significant percentage of ETEC diarrheal disease worldwide whether the disease presents as infant diarrhea with high mortality or as traveler's diarrhea. **CFA/I** pili (fimbriae) are virulence determinants that consist of repeating protein subunits (pilin), are found in several ETEC serogroups, and promote attachment to human intestinal mucosa. While **CFA/I** pili are highly immunogenic, the antigenic determinants of **CFA/I** have not been defined. We wished to identify the linear B-cell epitopes within the **CFA/I** molecule as determined by primate response to the immunizing protein. To do this, we (i) resolved the discrepancies in the literature on the complete amino acid sequence of **CFA/I** by N-terminal and internal protein sequencing of purified and selected proteolytic fragments of **CFA/I**, (ii) utilized this sequence to synthesize 140 overlapping octapeptides covalently attached to polyethylene pins which represented the entire **CFA/**

I protein, (iii) immunized three rhesus monkeys with multiple intramuscular injections of purified **CFA/I** subunit in Freund's adjuvant, and (iv) tested serum from each monkey for its ability to recognize the octapeptides in a capture enzyme-linked immunosorbent assay. Eight linear B-cell epitopes were identified; the region containing an epitope at amino acids 11 to 21 was strongly recognized by all three individual rhesus monkeys, while the amino acid stretches 22 to 29, 66 to 74, 93 to 101, and 124 to 136 each contained an epitope that was recognized by two of the three rhesus monkeys. The three other regions containing epitopes were recognized by one of the three individuals. The monkey antiserum to pilus subunits recognized native intact pili by immunogold labeling of **CFA/I** pili present on whole H10407 cells. Therefore, immunization with pilus subunits induces antibody that clearly recognizes both synthetic linear epitopes and intact pili. We are currently studying the importance of these defined epitope-containing regions as vaccine candidates.

FILE 'CAPLUS' ENTERED AT 16:27:22 ON 16 JUN 2000
L25 1 S SAVALTYS
L26 0 S L25 NOT (L2 OR L6)

FILE 'MEDLINE, BIOSIS, EMBASE, LIFESCI, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 16:27:57 ON 16 JUN 2000
L27 2 S L25
L28 1 S L27 NOT L13

L28 ANSWER 1 OF 1 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1998-145348 [13] WPIDS
DOC. NO. NON-CPI: N1998-114990
DOC. NO. CPI: C1998-047511
TITLE: Peptide(s) responsive to antibodies against Escherichia coli CS4-CFA/I family proteins - are subunits of consensus peptide useful for immunisation, and consequent antibody compositions, useful in assays and treatment of infection.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): CASSELS, F; LOOMIS-PRICE, L
PATENT ASSIGNEE(S): (USSA) US DEPT OF THE ARMY
COUNTRY COUNT: 20
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9805348	A1	19980212	(199813)*	EN	19

RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP

Searcher : Shears 308-4994

EP 959895 A1 19991201 (200001) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9805348	A1	WO 1997-US13476	19970801
EP 959895	A1	EP 1997-936322	19970801
		WO 1997-US13476	19970801

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 959895	A1	Based on	WO 9805348

PRIORITY APPLN. INFO: US 1996-23145 19960805; US 1996-23076 19960802

AN 1998-145348 [13] WPIDS

AB WO 9805348 A UPAB: 19980330

A peptide of at most 20 amino acids containing at least 1 of sequences (I)-(IV) is new:**SAVALTYS** (I) PSAVALTYSP (II) ASVDPTIDLLQA (III) TVTASVDPTIDLLQAD (IV) Also claimed are: (1) compositions containing at least 1 16-30 amino acid peptide from (I)-(IV) or 16 other sequences listed below, plus a pharmaceutically acceptable carrier: EKNITVTA; KNITVTAS; NITVTASV; ITVTASVD; TASVDPTI; ASVDPTID; SVDPTIDL; VDPTIDLL; DPTIDLLQ; PTIDLLQA; SALPSAVA; ALPSAVAL; LPSAVALT; PSAVALTY; AVALTYSP; VALTYSPA; and (2) compositions containing antibodies binding to a site containing (III).

The antibody composition is preferably in a carrier suitable for application to bacteria-containing growth media, or a pharmaceutically acceptable carrier (e.g. saline). The antibody preferably has a tag (e.g. a fluorescing agent or colorometric tag) to assist identification of antibody/E. coli CS4-CFA/I family protein complex.

USE - The peptides and compositions containing peptides are useful for immunisation to raise antibodies to organisms producing the CS4-CFA/I family of proteins; sequences (III) and (IV) are especially useful, since they should react with most antibodies of natural organisms producing CS4-CFA/I proteins. The CS4-CFA/I family belong to the enterotoxigenic (ETEC) class of Escherichia coli, one of five classes of E. coli causing diarrhoea. ETEC are the most common class and cause high infant mortality and illness in adult travellers in developing countries. The peptides are also useful to determine whether individual animals have antibodies to ETEC E. coli.The antibody compositions can be used in assays to detect organisms bearing the CS4-CFA/I family proteins, in which a culture

of organisms is contacted with the composition for sufficient time for interaction to occur, and the culture is examined to determine if a CS4-CFA/I family protein/antibody complex has formed (claimed). Kits for undertaking the assay are provided (not claimed). The antibody compositions can also be used to treat, or immunise a susceptible host against, illness arising from infection with bacteria bearing CS4-CFA/I family proteins, by administering a bacteria-agglutinating effective amount, optionally with an adjuvant (claimed).
Dwg.0/0

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FILE 'HOME' ENTERED AT 16:29:29 ON 16 JUN 2000